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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/598,781	09/11/2006	Anja Fecher	66535.000014	1292
21967 7590 02/03/2010 HUNTON & WILLIAMS LLP INTELLECTUAL PROPERTY DEPARTMENT 1900 K STREET, N.W. SUITE 1200 WASHINGTON, DC 20006-1109			EXAMINER STOCKTON, LAURA LYNN	
			ART UNIT	PAPER NUMBER
			1626	
			MAIL DATE	DELIVERY MODE
			02/03/2010	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

**Application No.**

10/598,781

**Applicant(s)**

FECHER ET AL.

**Examiner**

Laura L. Stockton

**Art Unit**

1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 13 October 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 4-13 and 16-24 is/are pending in the application.
- 4a) Of the above claim(s) 13, 18 and 21-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 4-12, 16, 17, 19 and 20 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB06)  
Paper No(s)/Mail Date See Continuation Sheet
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ ~~Notes of Informal Patent Application~~
- 6) ☐ Other: \_\_\_\_\_

Continuation of Attachment(s) 3. Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :  
October 17, 2006 and March 9, 2007.

**DETAILED ACTION**

**Claims 4-13 and 16-24 are pending in the application.**

***Election/Restrictions***

Applicant's election with traverse of Group I (products of formula I or products of formula I<sub>C1</sub> or products of formula I<sub>C2</sub>) in the reply filed on October 13, 2009 is acknowledged. The traversal is on the ground(s) that elected Group I, as amended, is drawn to products and Group II are drawn to methods of using the products of Group I. This is not found persuasive because unity is lacking since the special technical feature, the 3-oxo-1-propen-1-yl-1H-indole-1-acetic acid core, does not define a contribution over the prior art as stated in the Restriction Requirement of September 4, 2009 and as shown below in the rejection under 35 USC 103.

The requirement is still deemed proper and is therefore made FINAL.

Claims 13, 18 and 21-24 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on October 13, 2009.

***Priority***

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

***Information Disclosure Statement***

The Examiner has considered the Information Disclosure Statement filed on October 17, 2006 and March 9, 2007.

***Claim Objections***

Claim 11 is objected to because of the following informalities: in the 5th line from the end of the claim, "R<sub>6</sub>" should be changed to "R<sup>6</sup>". Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16 and 17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an enantiomer, racemate, diastereoisomer, a pharmaceutical acceptable salt or prodrug of compounds of formula I<sub>C1</sub> or I<sub>p</sub> does not reasonably provide enablement for a solvate, geometric isomer, meso form, morphological form of a compounds of formula

I<sub>c1</sub> or I<sub>p</sub>. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in making an enablement rejection are summarized as:

- a) the quantity of experimentation necessary,
- b) the amount of direction or guidance presented,
- c) the presence or absence of working examples,
- d) the nature of the invention,
- e) the state of the prior art,
- f) the relative skill of those in the art,
- g) the predictability or unpredictability of the art, and
- h) the breadth of the claims.

In re Colianni, 195 USPQ 150 (CCPA 1977). In re Rainer, et al., 146 USPQ 218 (CCPA 1965). *Ex parte Formal*, 230 USPQ 546 (BPAI 1986).

a) Determining if a particular compound would form a solvate, for example, would require synthesis and recrystallization of the compound solvate or hydrate using a variety of solvents, temperatures and humidities. The experimentation for solvates is potentially open-ended.

b) The specification merely mentions the Applicant's intention to make solvates, without teaching the preparation thereof.

c) While the claims recite solvates, no working examples show their formation. As stated in Morton International Inc. v. Cardinal Chemical Co., 28 USPQ2d 1190, 1194 (Fed.Cir. 1993):

The specification purports to teach, with over fifty examples, the preparation of the claimed compounds ... However ... there is no evidence that such compounds exist ... [T]he examples ... do not produce the postulated compounds ... [T]here is ... no evidence that such compounds even exist.

The specification shows no evidence of the formation and actual existence of solvates. Hence,



Applicant must show formation of solvates, geometric isomers, meso forms, morphological forms or limit the claims accordingly.

d) The nature of the invention is chemical synthesis of solvates, which involves chemical reactions.

e) The state of the art recognizes that the formation, composition and therapeutic activity of solvates are unpredictable. The Federal Circuit has recognized a solvate as an example of a polymorph or pseudopolymorph (emphasis added):

"Polymorphs" are distinct crystalline structures containing the same molecules. These structural differences can affect various properties of the crystals, such as melting points and hardness (e.g., graphite and diamonds are both crystalline forms of carbon) .... [P]seudopolymorphs are often loosely called polymorphs ... Pseudopolymorphs not only have their molecules arranged differently but also have a slightly different molecular composition. A common type of pseudopolymorph is a solvate, which is a crystal in which the molecules defining the crystal structure "trap" molecules of a solvent. The crystal molecules

and the solvent molecules then bond to form an altered crystalline structure.

SmithKline Beecham Corp. v. Apotex Corp., 74 USPQ2d 1398, 1409 (Fed.Cir. 2005). The same rationale obtains for hydrates; solvates in which the solvent is water. Souillac, et al., Characterization of Delivery Systems, Differential Scanning Calorimetry, pages 217-218 (in Encyclopedia of Controlled Drug Delivery, 1999, John Wiley & Sons, pages 212-227), recognize that different polymorphs of the same drug can have different therapeutic activity (emphasis added):

Because different polymorphic forms of the same drug exhibit significant differences in their physical characteristics, therapeutic activity from one form to another may be different. Studying the polymorphism of a drug and the relative stability of the different polymorphs is a critical part of pre-formulation development.

Further, Vipagunta et al. (Advanced Drug Delivery Reviews, 48 (2001), pages 3-26) state "Predicting the formation of solvates or hydrates of a compound and the number of molecules of water or solvent incorporated in

to the crystal lattice of a compound is complex and difficult." See page 18, section 3.4.

f) The artisan using Applicant's disclosure to prepare the claimed solvates would be, e.g., an experienced process chemist with at least a BS chemistry degree.

g) Chemical reactions are known as unpredictable. In re Marzocchi, et al., 169 USPQ 367, 370 (CCPA 1971); In re Fisher, 166 USPQ 18, 24 (CCPA 1970). See above regarding the unpredictability of solvate formation.

h) The breadth of the claims includes thousands of compounds of the instant formulas  $I_{c1}$  and  $I_p$  as well as presently unknown compounds embraced by the terms solvates, geometric isomers, meso forms, morphological forms. See MPEP 2164.01(a), discussed supra, justifying the conclusion of lack of enablement commensurate with the claims. Undue experimentation will be required to practice Applicant's claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4-12, 16, 17, 19 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 is of unclear scope since it recites what is excluded and thus does not clearly define what is within applicant's invention. As stated in In re Schechter 98 USPQ 144, such limitations in a claim renders it indefinite "since applicant sought to claim what was not invented, rather than "particularly and distinctly pointing out" what was invented.". See page 147.

In claim 5, the R<sup>5</sup> and R<sup>6</sup> variables being substituted lacks antecedent basis from claim 4 since it is not stated in claim 4 that substituents

represented by these variables are optionally substituted. See claim 10 for same.

In claim 10, there are species listed in dependent claim 10 which have been excluded per the proviso at the end of claim 4. See, for example, the ninth compound listed on page 5 in claim 10 and the first compound listed under the proviso on page 3 in claim 4.

In claim 10, the 19th compound listed on page 5, the nomenclature of this species is unclear as to its meaning (e.g., "352'").

In claim 16, the possible substituents substituted on the aryl group under the definition of variables  $R^5$  and  $R^6$  is much different in scope than that which is stated under the definition of the term "aryl" at the end of the claim (page 13). Therefore, claim 16 is indefinite.

Dependent claim 17 lacks antecedent basis from independent claim 4 since it is not stated in claim 4

that the compound of formula Ic can be in any other form other than the base form or a salt thereof.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 4, 6-9, 11, 12, 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dinnell et al. {US 2001/0039286} and Maruyama et al. {WO 03/037862}, each taken alone. Since the WO is in a non-English language, the US equivalent, US 2005/0014942, will be referred to hereinafter.

***Determination of the scope and content of the prior art (MPEP***

***§2141.01)***

Applicant claims indole compounds. **Dinnell et al.** (see entire document; particularly pages 1, 4 and 5; and especially Example 46 on page 28) and **Maruyama et al.** (see entire document; particularly pages 1-4 and 7; and especially Example 2 on page 17) each teach indole compounds that are structurally similar to the instant claimed compounds.

***Ascertainment of the difference between the prior art and the claims***  
***(MPEP §2141.02)***

The difference between the compounds of the prior art and the compounds instantly claimed is that the instant claimed compounds are generically described in the prior art.

***Finding of prima facie obviousness--rational and motivation (MPEP***  
***§2142-2413)***

The indiscriminate selection of "some" among "many" is *prima facie* obvious, In re Lemin, 141 USPQ 814 (C.C.P.A. 1964). The motivation to make the claimed compounds derives from the expectation that

structurally similar compounds would possess similar activity (e.g., treating rheumatoid arthritis).

One skilled in the art would thus be motivated to prepare products embraced by the prior art to arrive at the instant claimed products with the expectation of obtaining additional beneficial products which would be useful in treating, for example, rheumatoid arthritis. The instant claimed invention would have been suggested to one skilled in the art and therefore, the instant claimed invention would have been obvious to one skilled in the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura L. Stockton whose telephone number is (571) 272-0710. The examiner can normally be reached on Monday-Friday from 6:00 am to 2:30 pm. If the examiner is out of the Office, the examiner's supervisor, Joseph McKane, can be reached on (571) 272-0699.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for



published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

The Official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

/Laura L. Stockton/  
Laura L. Stockton  
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February 4, 2010